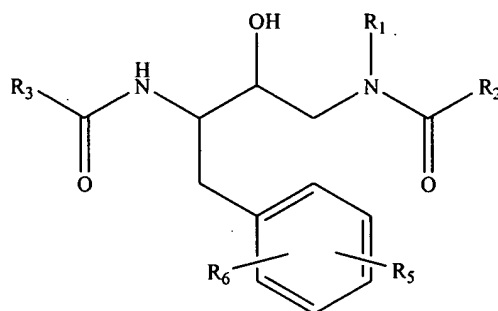


Amendments to the Claims:

This listing of claims will replace all prior versions, and listings of claims in the application:

Listing of Claims:

1 (currently amended): A method for modulating the processing of an amyloid precursor protein (APP), said method comprising contacting a composition containing said APP with an aspartyl protease inhibitor having the ~~general~~ formula:



(I)

wherein:

R₁, R₂ and R₃ are members independently selected from the group consisting of alkyl, substituted alkyl, aryl, substituted aryl, arylalkyl, substituted arylalkyl, aryloxyalkyl, substituted aryloxyalkyl, heteroaryl, substituted heteroaryl, heteroarylalkyl, substituted heteroarylalkyl, heterocycles, substituted heterocycles, heterocyclicalkyl and substituted heterocyclicalkyl; and

R₅ and R₆ are independently selected from the group consisting of hydrogen, halogen, alkyl, substituted alkyl, aryl, substituted aryl, arylalkyl, substituted arylalkyl, aryloxyalkyl and substituted aryloxyalkyl; or R₅ and R₆ and the carbons to which they are bound join to form an optionally

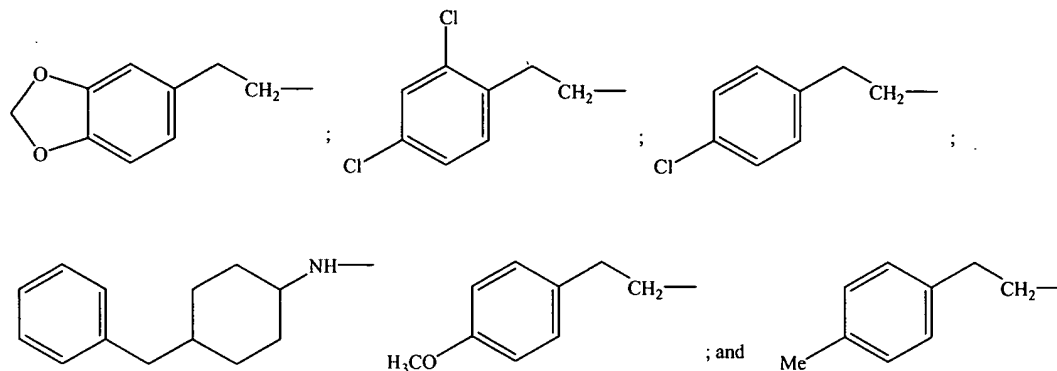
17 substituted carbocyclic or heterocyclic fused ring system having a total of
18 9- or 10-ring atoms within said fused ring system.

1 2 (original): The method according to claim 1, wherein:

2 R₁ is a member selected from the group consisting of substituted alkylaryl,
3 substituted aryl, substituted alkyl and substituted heterocyclic groups.

1 3 (original): The method according to claim 2, wherein:

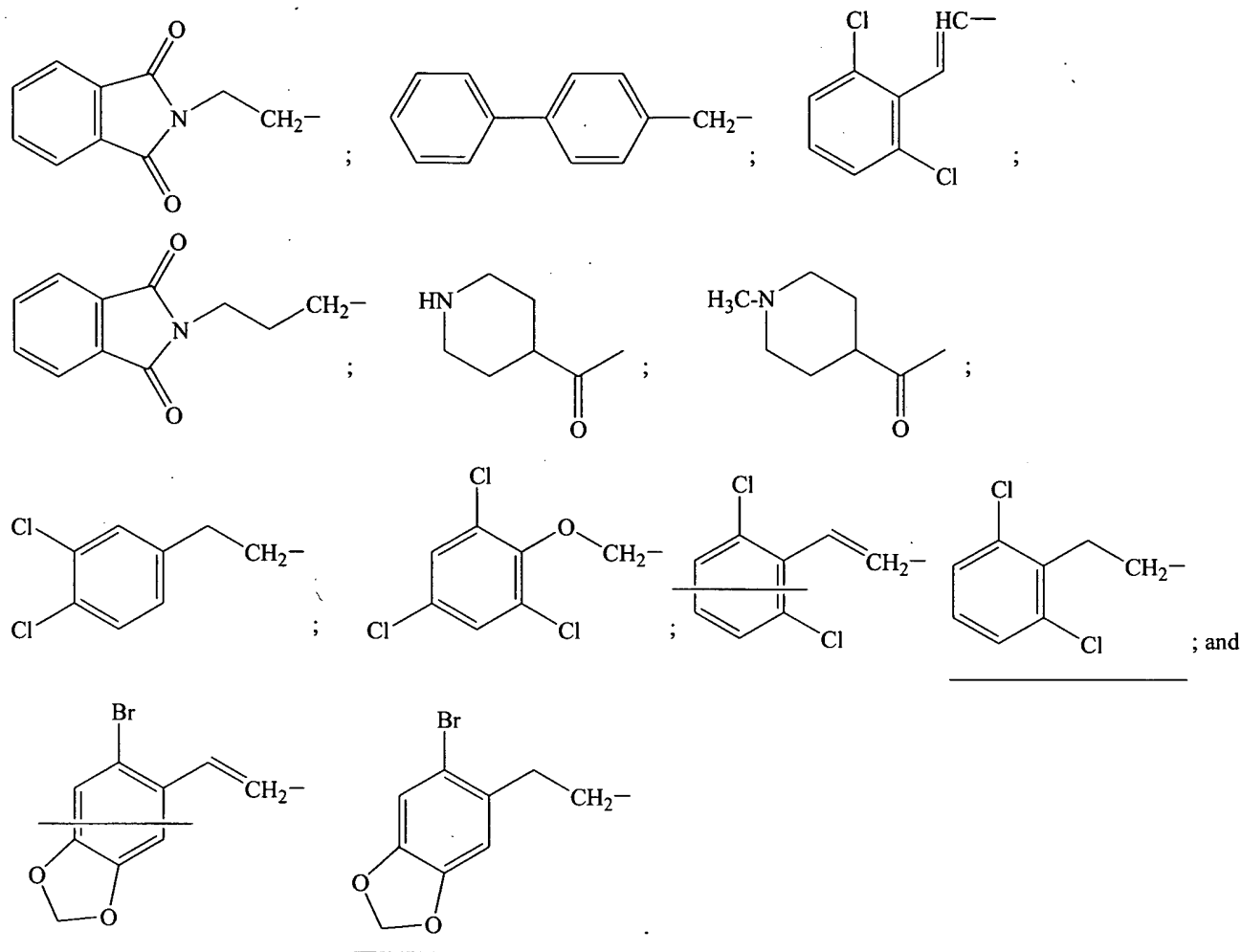
2 R₁ is a member selected from the group consisting of:



3 4 (original): The method according to claim 1, wherein:

4 R₂ is a member selected from the group consisting of substituted alkyl,
5 heterocyclic and substituted heterocyclic groups.

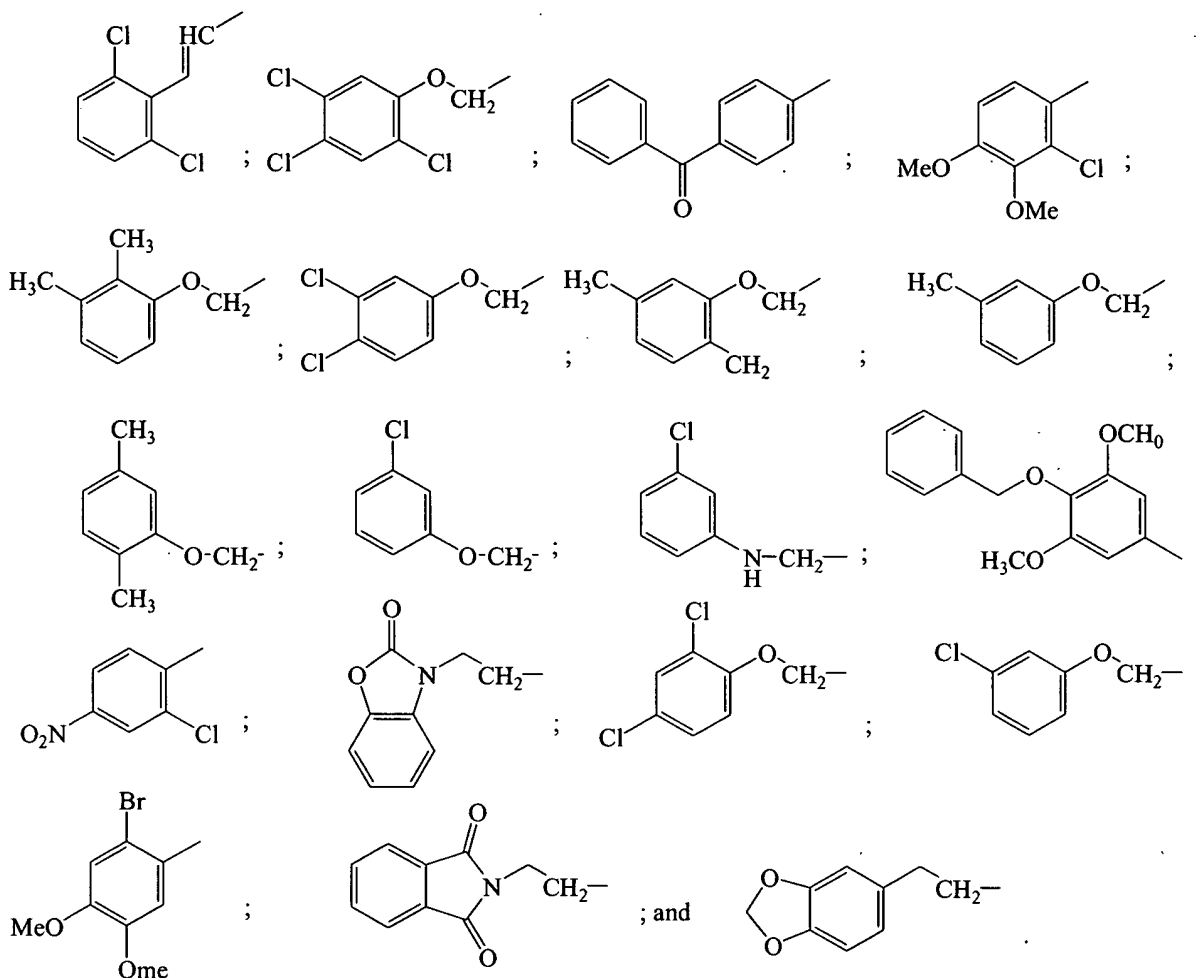
1 5 (currently amended): The method according to claim 4, wherein R₂ is a
2 member selected from the group consisting of:



3
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1 6 (original): The method according to claim 1, wherein:
2 R₃ is a member selected from the group consisting of substituted alkyl and
3 substituted aryl groups.

1 7 (original): The method according to claim 6, wherein R₃ is a member selected
2 from the group consisting of:

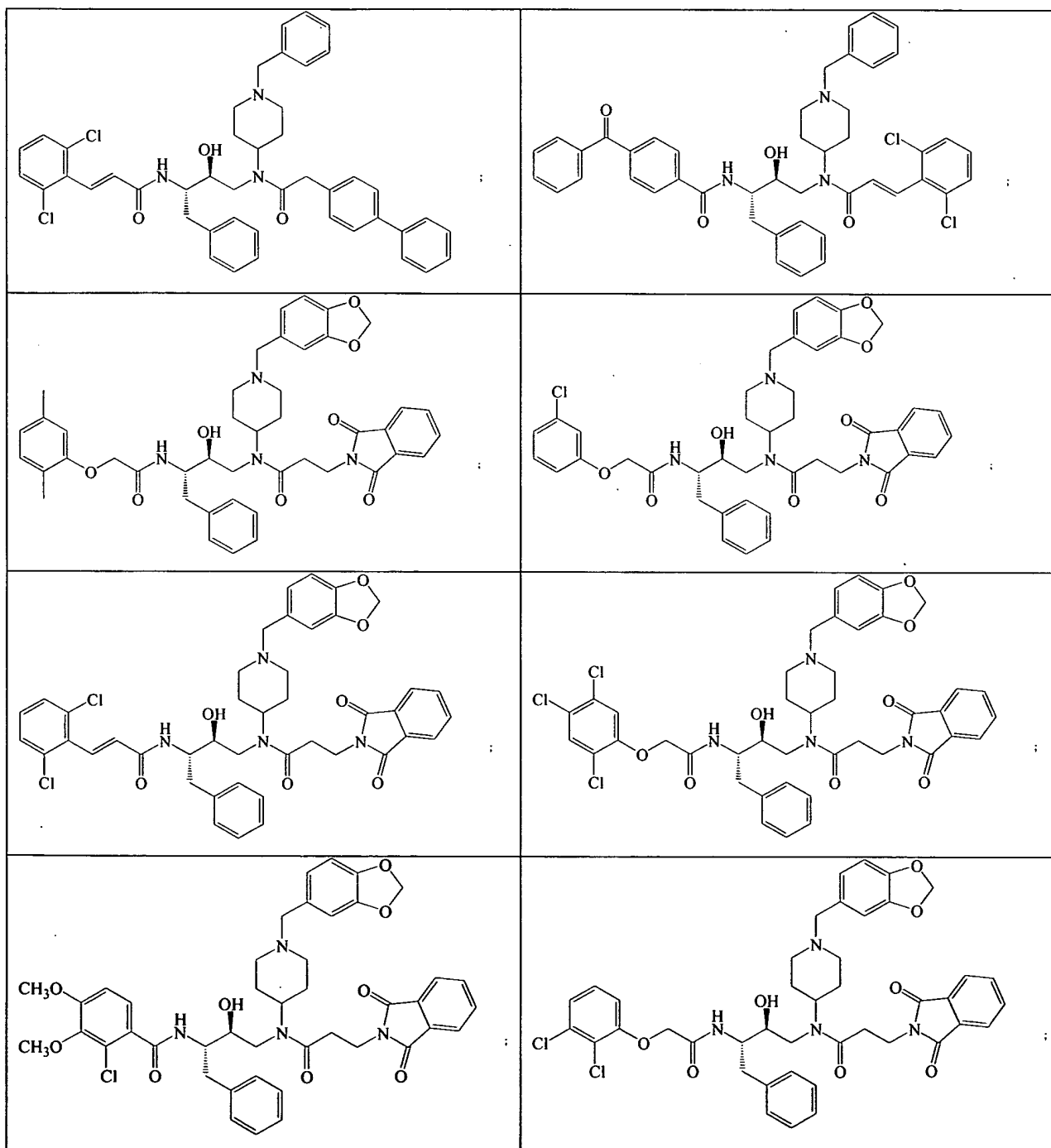


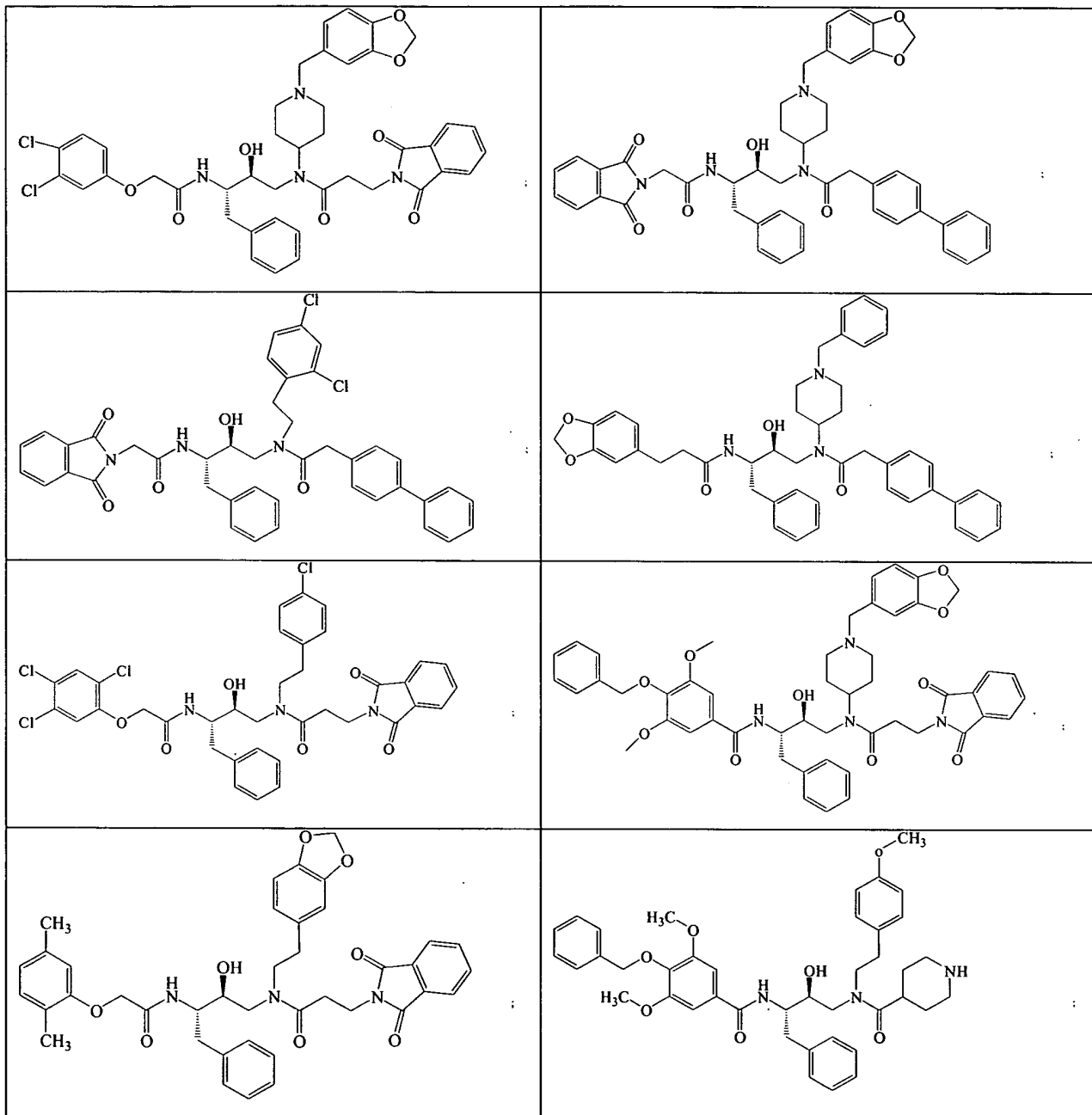
8 (original): The method according to claim 1, wherein R₅ and R₆ and the carbons to which they are bound form an optionally substituted naphthalene ring.

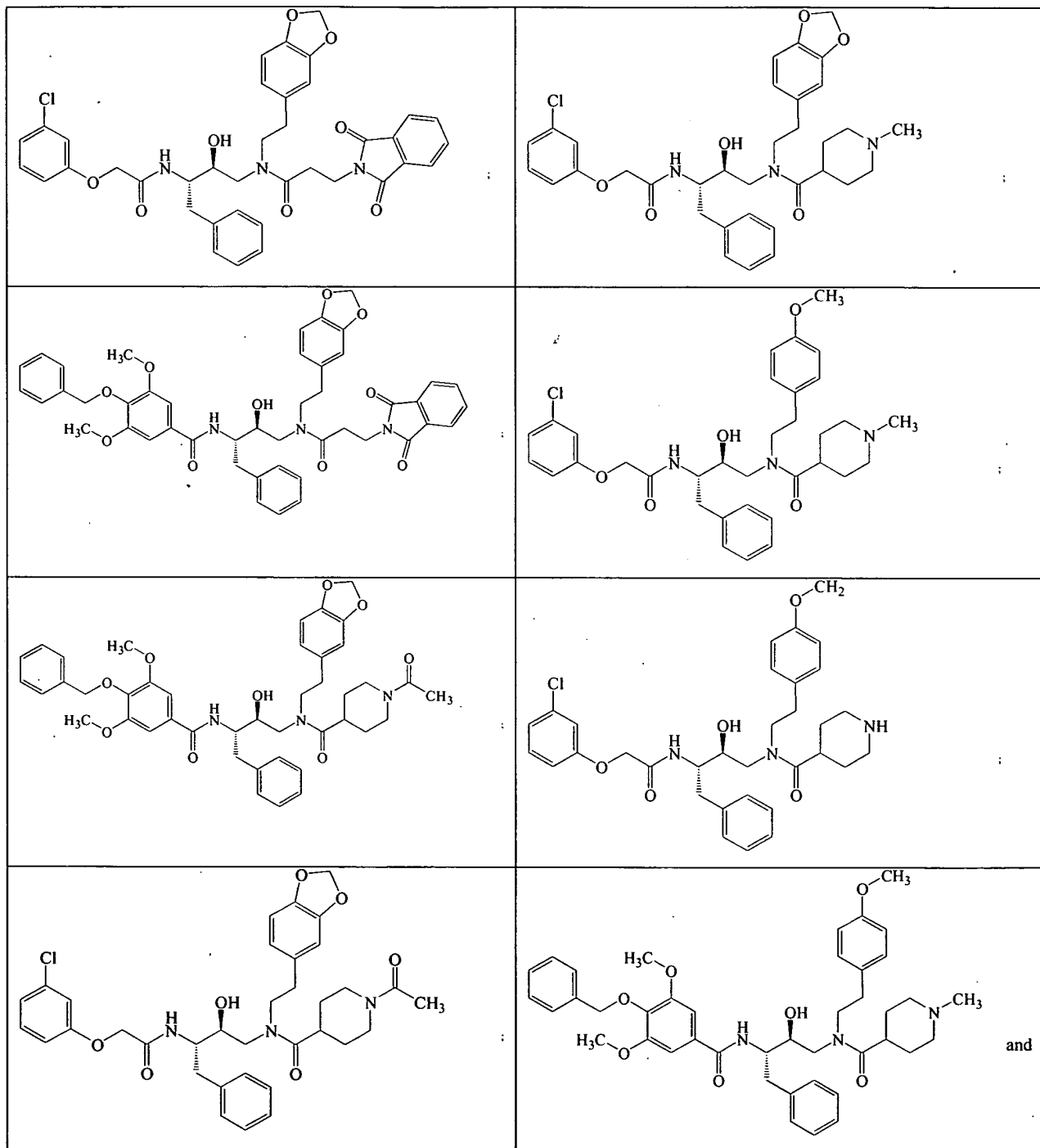
9 (original): The method according to claim 1, wherein R₅ and R₆ are both hydrogen.

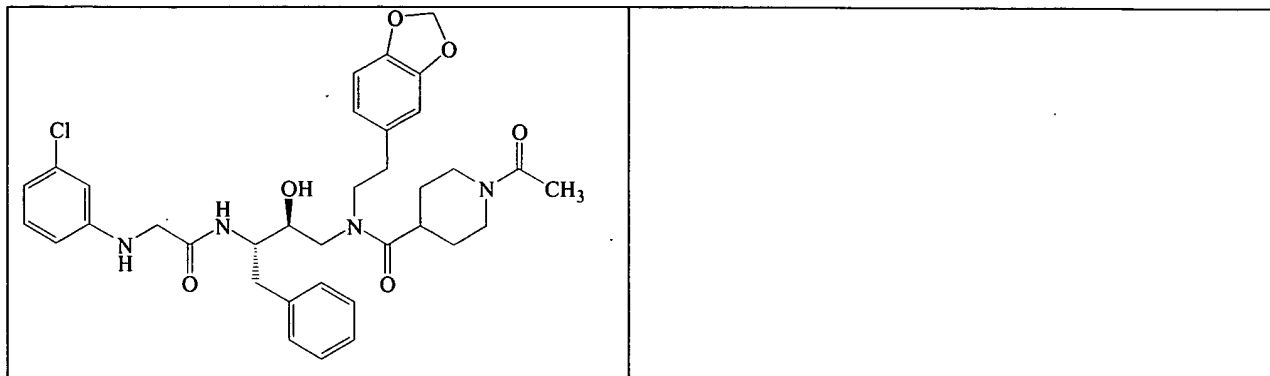
10 (original): The method in accordance with claim 1, wherein R₅ is hydrogen and R₆ is meta or para to R₅ and is a member selected from the group consisting of halogen, alkyl, substituted alkyl, aryl, substituted aryl, arylalkyl, substituted arylalkyl, aryloxyalkyl and substituted aryloxyalkyl.

- 1 11 (original): The method according to claim 1, wherein said aspartyl protease
2 inhibitor is a member selected from the group consisting of:





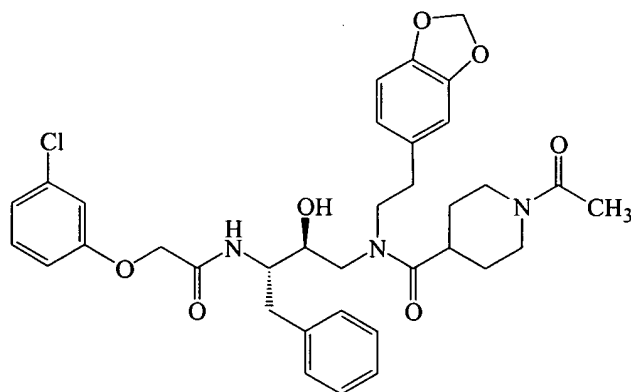




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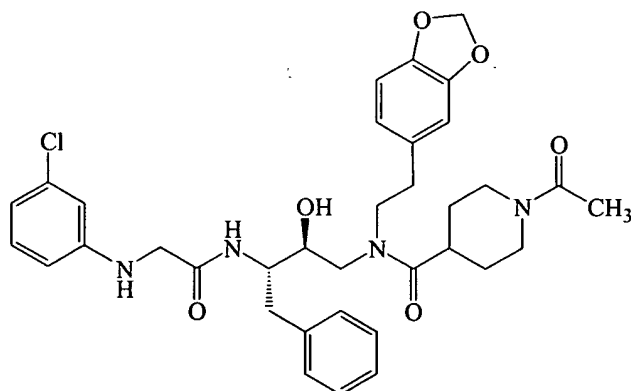
4

1 12 (original): The method according to claim 1, wherein said aspartyl protease
2 inhibitor is a member selected from the group consisting of:



3

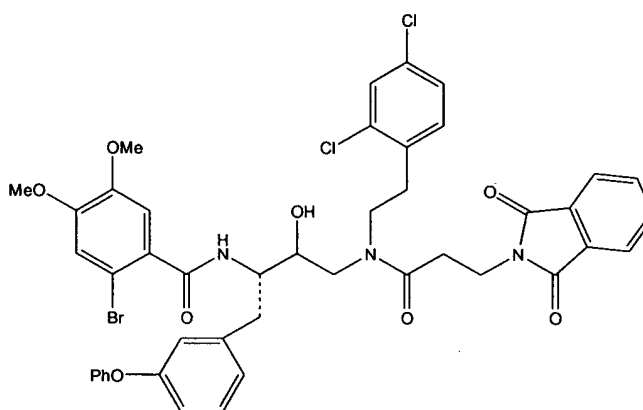
and



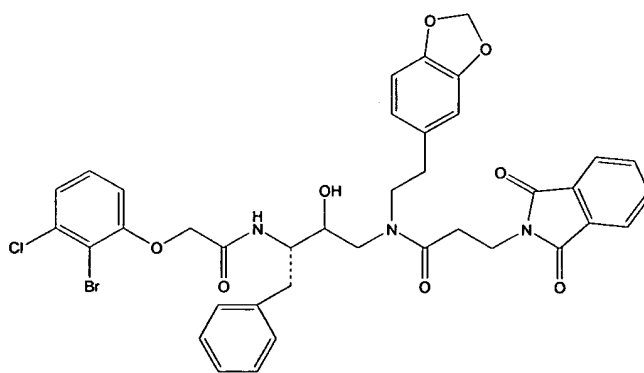
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13 (currently amended): The method in accordance with claim 1, wherein said
aspartyl protease inhibitor is a member selected from the group consisting of CEL5-A, CEL5-G
and EA-1, which are illustrated in FIG. 12

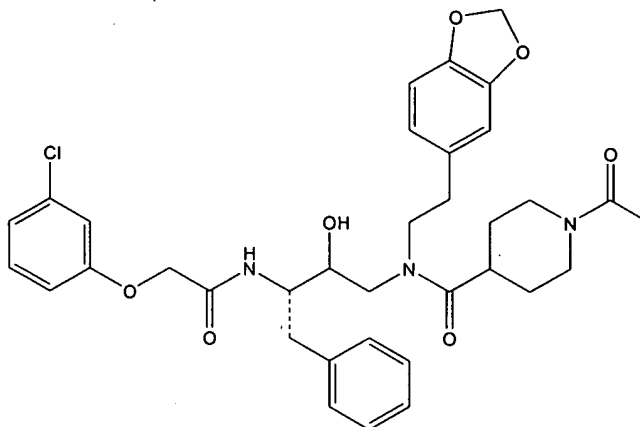
CEL5-A having the following structure:



CEL5G having the following structure:



EA 1 having the following structure:



9

1 14 (original): The method in accordance with claim 1, wherein said composition
2 is a body fluid.

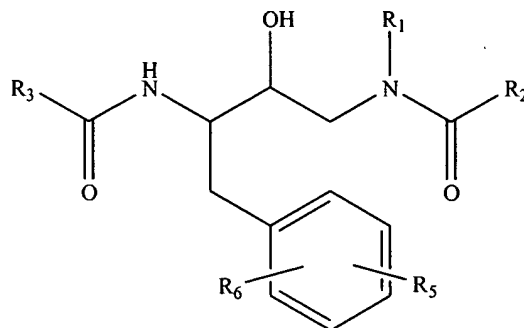
1 15 (currently amended): The method in accordance with claim [[13,]] 14,
2 wherein said body fluid is cerebral spinal fluid.

1 16 (original): The method in accordance with claim 1, whereby formation of
2 amyloidogenic A β peptides (A β) is decreased compared to the amount formed in the absence of
3 said aspartyl protease inhibitor.

1 17 (original): The method in accordance with claim 1, whereby formation of α -
2 sAPP is increased compared to the amount formed in the absence of said aspartyl protease
3 inhibitor.

1 18 (original): The method in accordance with claim 1, wherein the modulation is
2 effected by modulating the activity of cathepsin D.

1 19 (currently amended): A method for modulating the processing of a tau-
2 protein (τ -protein), said method comprising contacting a composition containing said τ -protein
3 with an aspartyl protease inhibitor having the ~~general~~ formula:



(I)

wherein:

R_1 , R_2 and R_3 are members independently selected from the group consisting of alkyl, substituted alkyl, aryl, substituted aryl, arylalkyl, substituted arylalkyl, aryloxyalkyl, substituted aryloxyalkyl, heteroaryl, substituted heteroaryl, heteroarylalkyl, substituted heteroarylalkyl, heterocycles, substituted heterocycles, heterocyclicalkyl and substituted heterocyclicalkyl; and

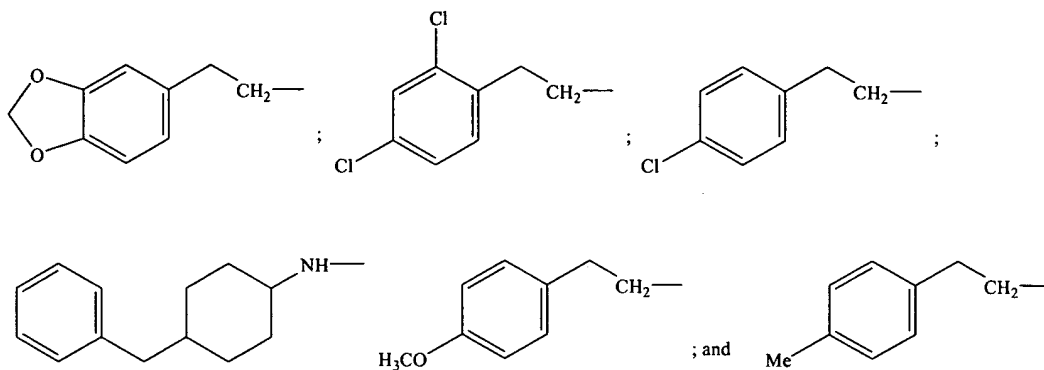
R_5 and R_6 are independently selected from the group consisting of hydrogen, halogen, alkyl, substituted alkyl, aryl, substituted aryl, arylalkyl, substituted arylalkyl, aryloxyalkyl and substituted aryloxyalkyl; or R_5 and R_6 and the carbons to which they are bound join to form an optionally substituted carbocyclic or heterocyclic fused ring system having a total of 9- or 10-ring atoms within said fused ring system.

20 (original): The method according to claim 19, wherein:

R_1 is a member selected from the group consisting of substituted alkylaryl, substituted aryl, substituted alkyl and substituted heterocyclic groups.

21 (original): The method according to claim 20, wherein:

R_1 is a member selected from the group consisting of:



3

1

22 (original): The method according to claim 19, wherein:

2

R₂ is a member selected from the group consisting of substituted alkyl,

3

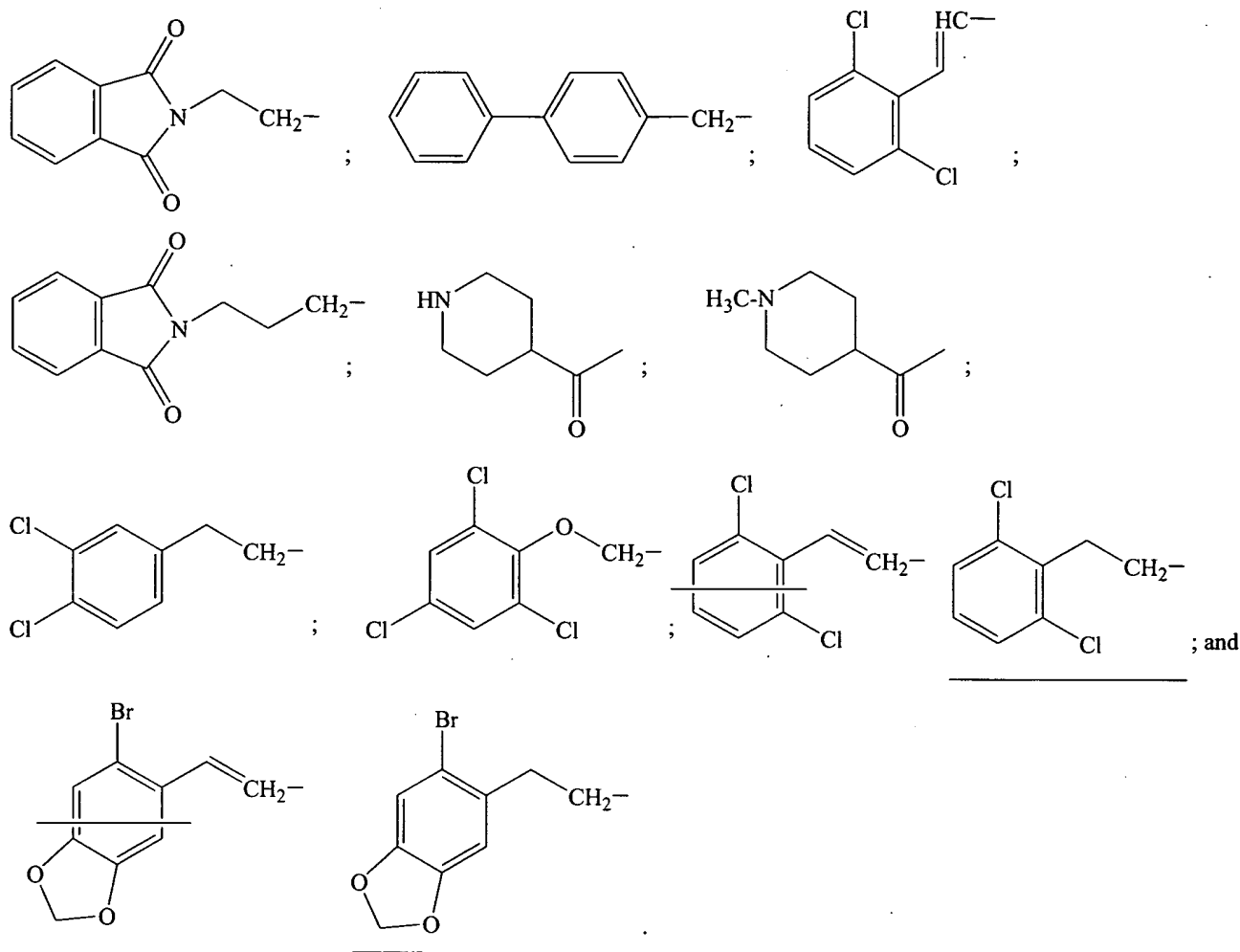
heterocyclic and substituted heterocyclic groups.

1

23 (currently amended): The method according to claim 22, wherein R₂ is a

2

member selected from the group consisting of:

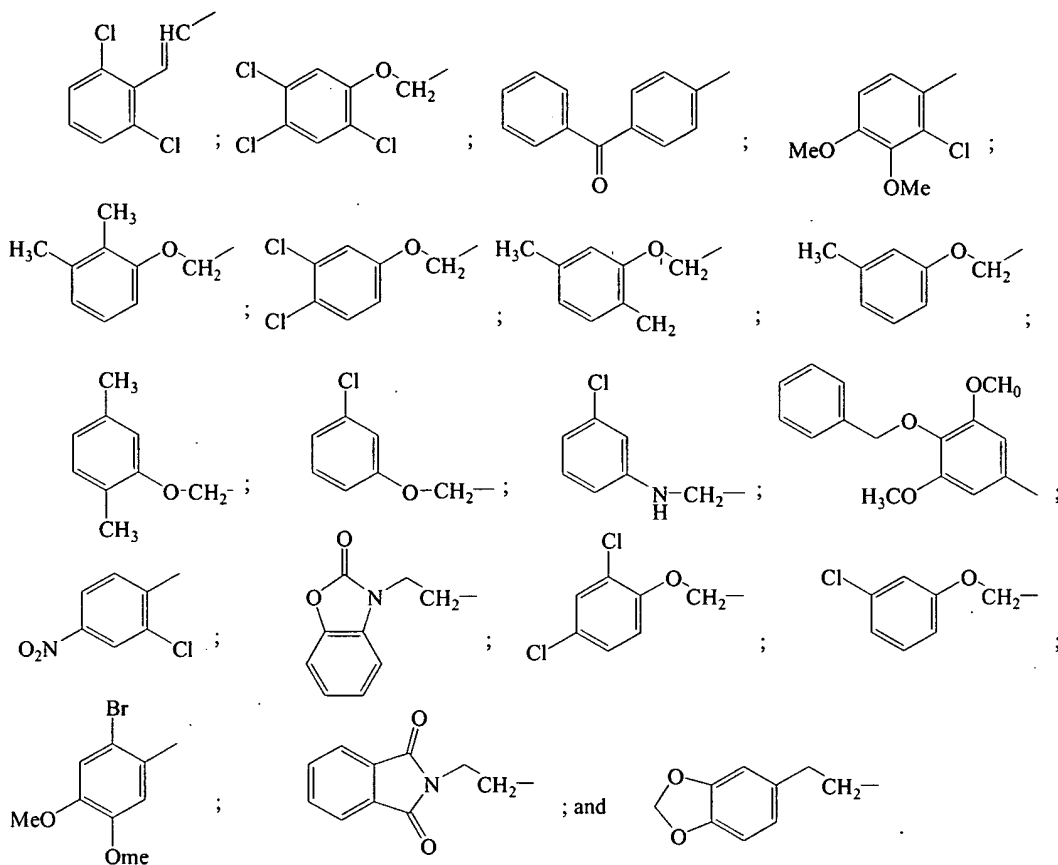


24 (original): The method according to claim 19, wherein:

R₃ is a member selected from the group consisting of substituted alkyl and substituted aryl groups.

25 (original): The method according to claim 24, wherein R₃ is a member

selected from the group consisting of:

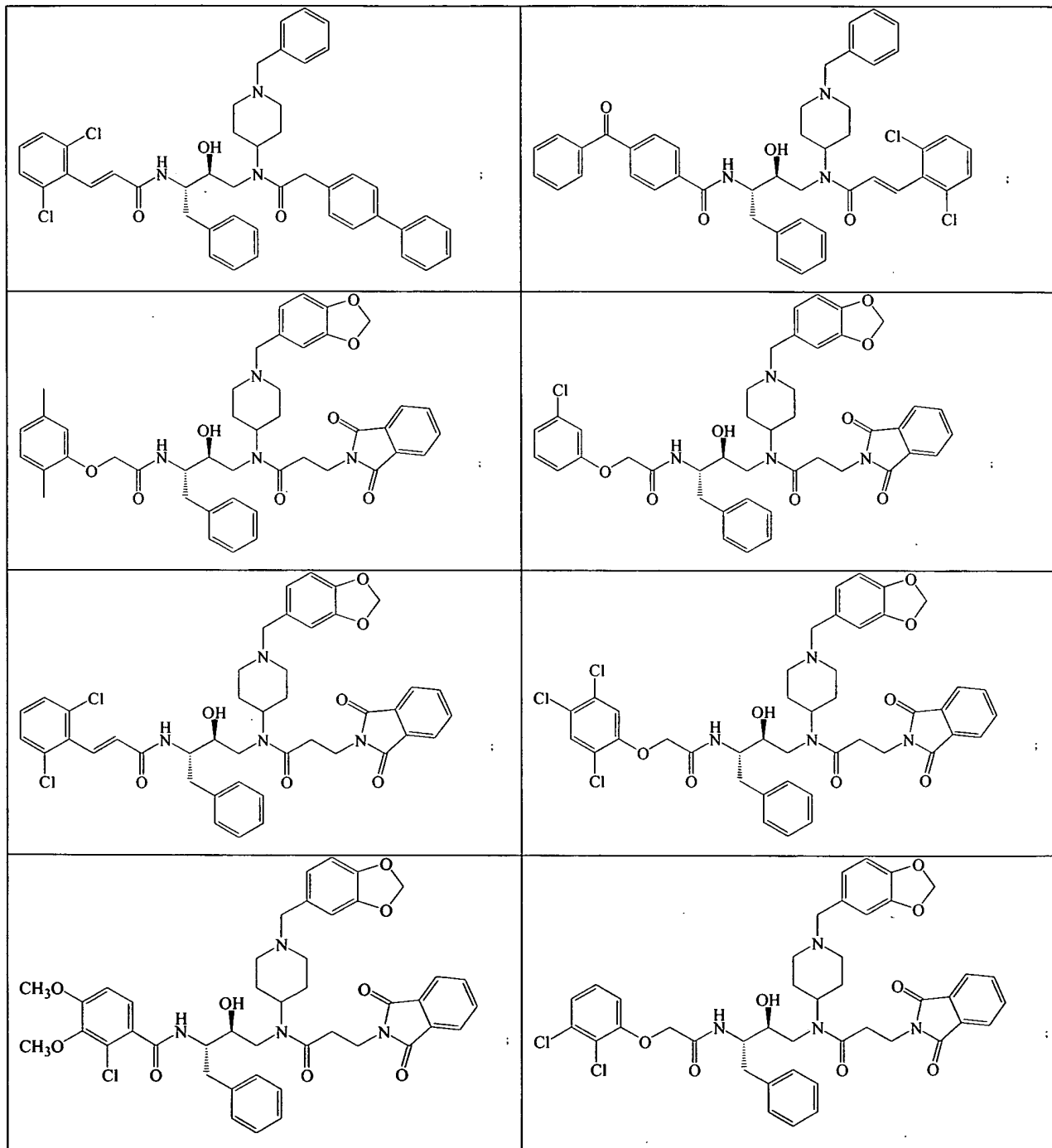


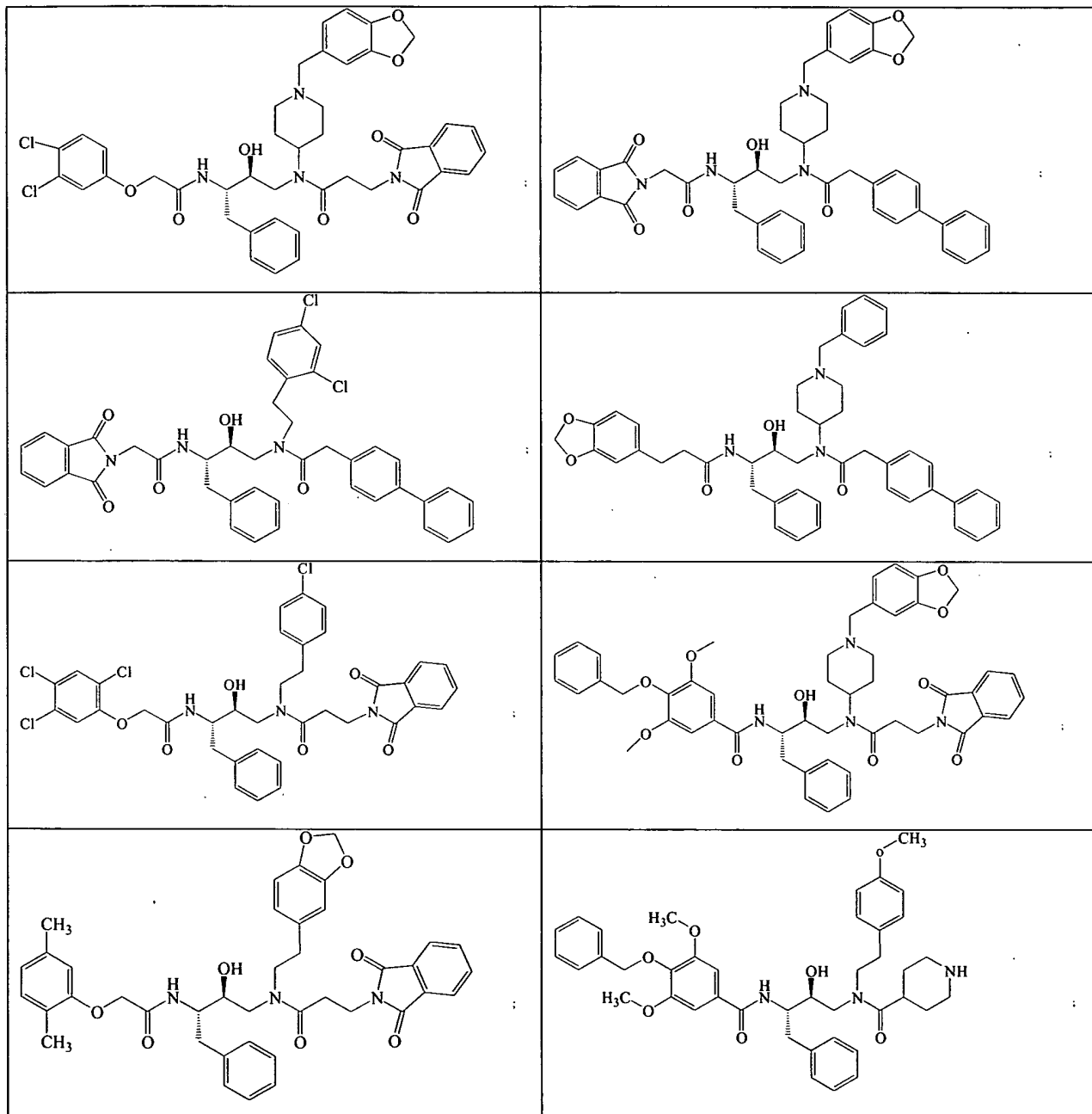
26 (original): The method according to claim 19, wherein R₅ and R₆ and the carbons to which they are bound form an optionally substituted naphthalene ring.

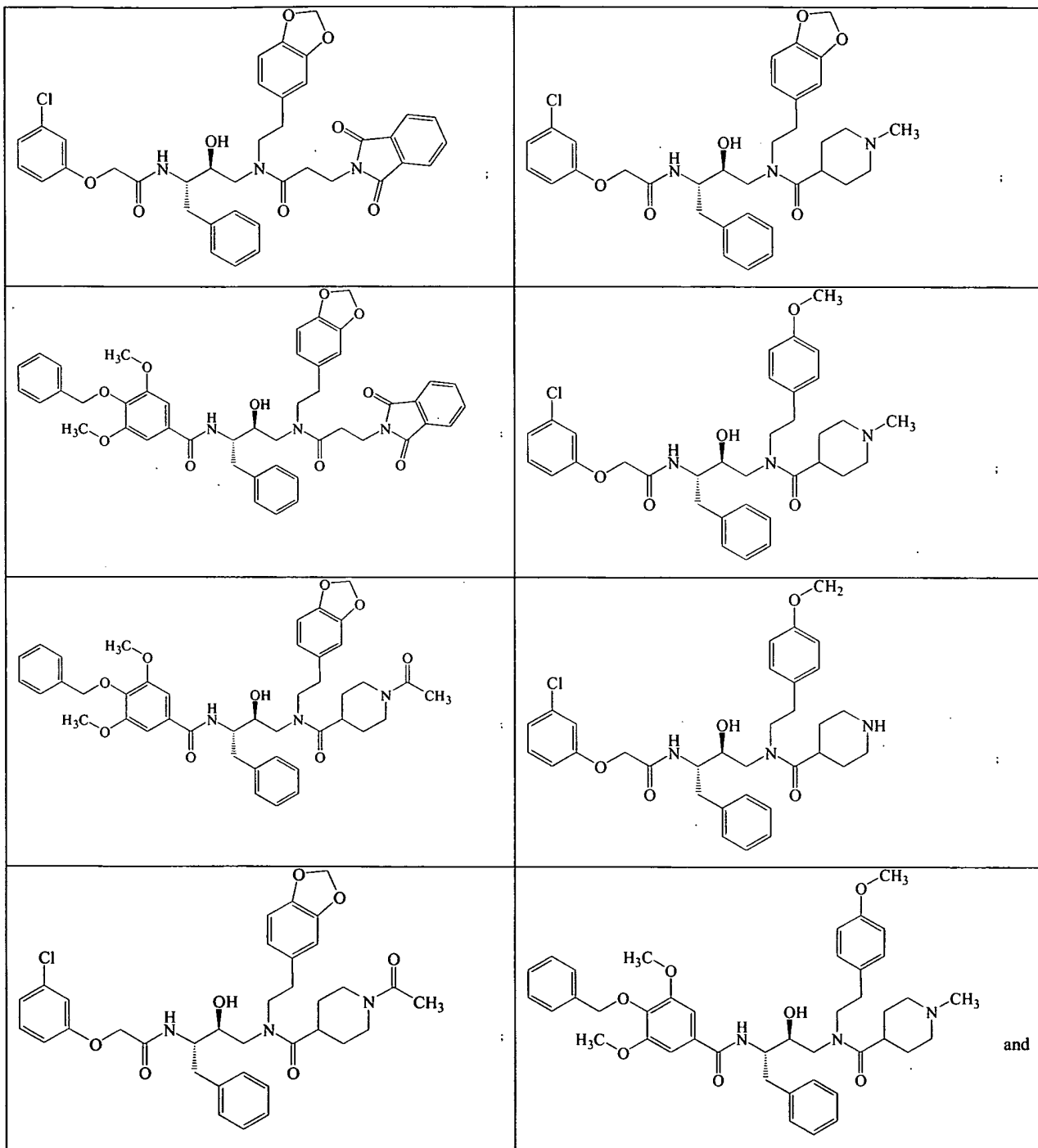
27 (original): The method according to claim 19, wherein R₅ and R₆ are both hydrogen.

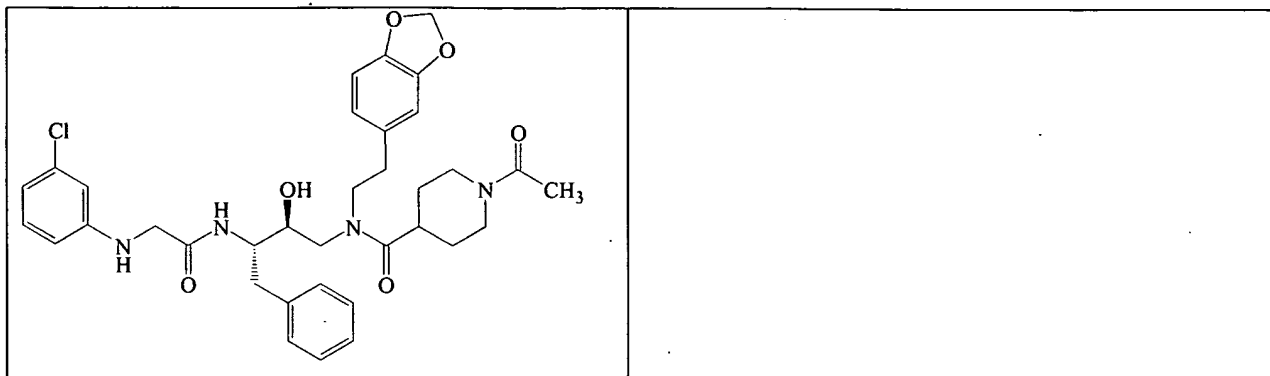
28 (original): The method in accordance with claim 19, wherein R₅ is hydrogen and R₆ is meta or para to R₅ and is a member selected from the group consisting of halogen, alkyl, substituted alkyl, aryl, substituted aryl, arylalkyl, substituted arylalkyl, aryloxyalkyl and substituted aryloxyalkyl.

29 (original): The method according to claim 19, wherein said aspartyl protease inhibitor is a member selected from the group consisting of:





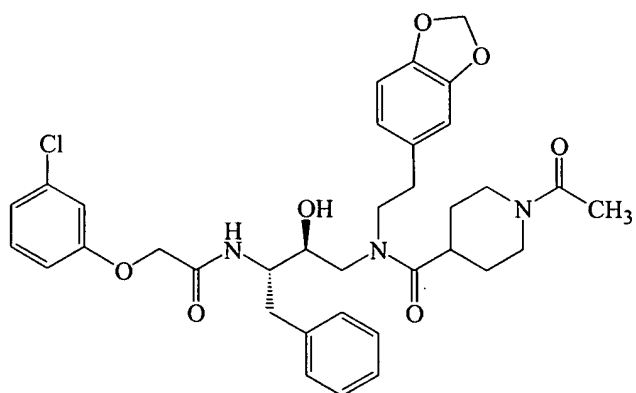




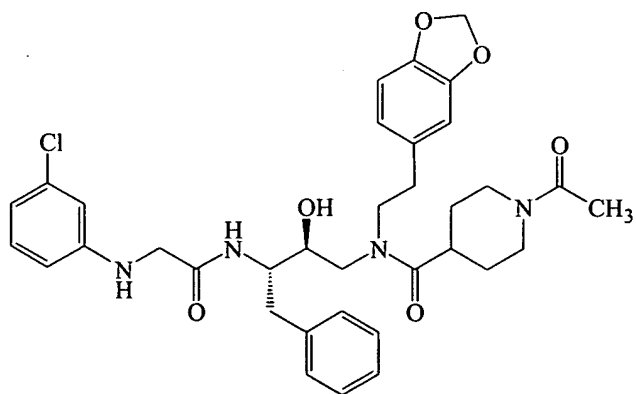
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1 30 (original): The method according to claim 19, wherein said aspartyl protease

2 inhibitor is a member selected from the group consisting of:

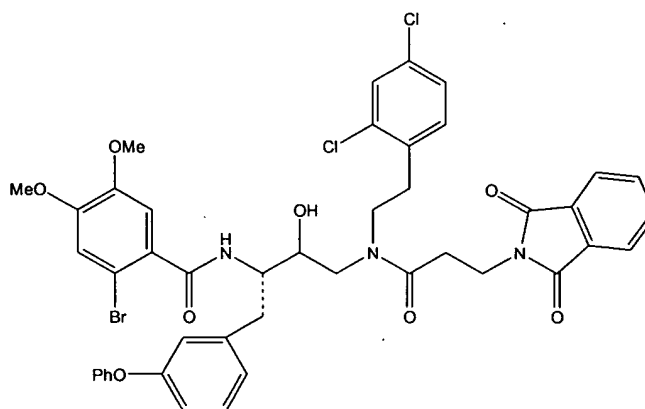


and

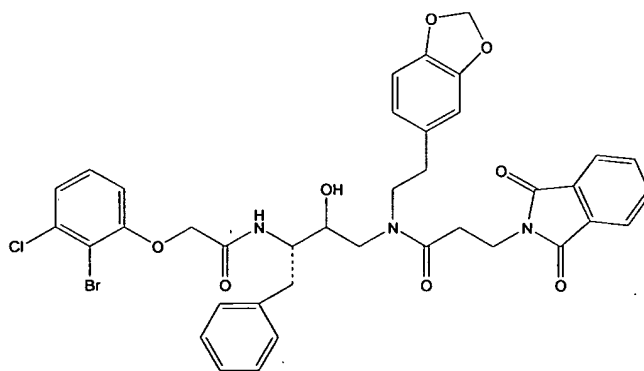


31 (currently amended): The method in accordance with claim 19, wherein said
aspartyl protease inhibitor is a member selected from the group consisting of ~~CEL5-A, CEL5-G~~
and ~~EA-1~~, which are illustrated in FIG. 12

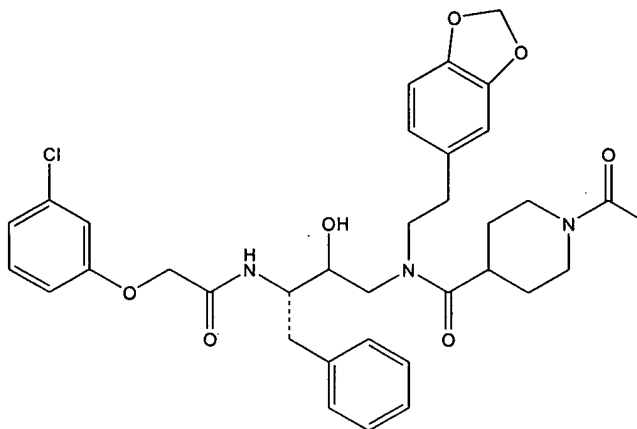
CEL5-A having the following structure:



CEL5G having the following structure:



EA 1 having the following structure:



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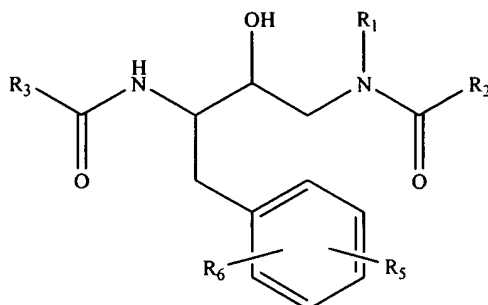
1 32 (original): The method in accordance with claim 19, wherein said
2 composition is a body fluid.

1 33 (currently amended): The method in accordance with claim [[31,]] 32,
2 wherein said body fluid is cerebral spinal fluid.

1 34 (original): The method in accordance with claim 19, whereby formation of τ -
2 fragments is decreased compared to the amount formed in the absence of said aspartyl protease
3 inhibitor.

1 35 (original): The method in accordance with claim 19, wherein the modulation
2 is effected by modulating the activity of cathepsin D.

1 36 (currently amended): A method for treating a neurodegenerative disorder,
2 said method comprising: administering to a mammal a therapeutically effective amount of an
3 aspartyl protease inhibitor having the ~~general~~ formula:



(I)

wherein:

R₁, R₂ and R₃ are members independently selected from the group consisting of alkyl, substituted alkyl, aryl, substituted aryl, arylalkyl, substituted arylalkyl, aryloxyalkyl, substituted aryloxyalkyl, heteroaryl, substituted heteroaryl, heteroarylalkyl, substituted heteroarylalkyl, heterocycles, substituted heterocycles, heterocyclicalkyl and substituted heterocyclicalkyl; and

R₅ and R₆ are independently selected from the group consisting of hydrogen, halogen, alkyl, substituted alkyl, aryl, substituted aryl, arylalkyl, substituted arylalkyl, aryloxyalkyl and substituted aryloxyalkyl; or R₅ and R₆ and the carbons to which they are bound join to form an optionally substituted carbocyclic or heterocyclic fused ring system having a total of 9- or 10-ring atoms within said fused ring system; and

a pharmaceutically acceptable carrier,

wherein: said neurodegenerative disorder is characterized by the accumulation of amyloid plaques or by the accumulation of the accumulation of τ -fragments.

37-38 (canceled)

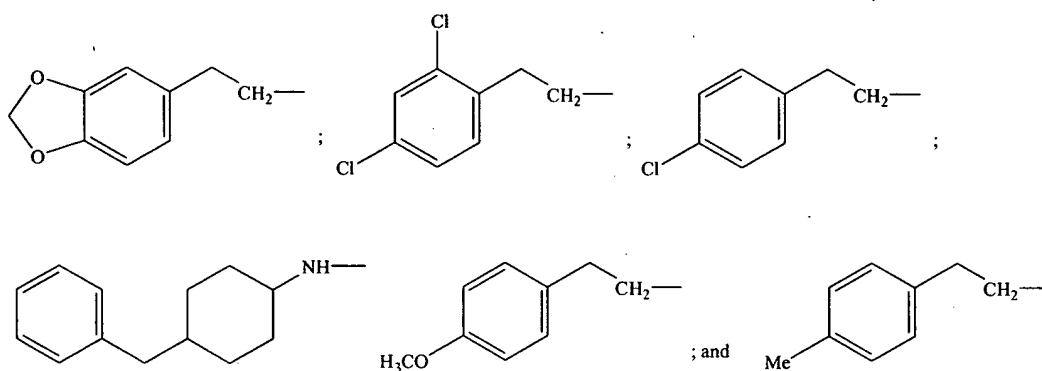
39 (original): The method in accordance with claim 36, wherein said neurodegenerative disorder is a member selected from the group consisting of Alzheimer's disease, Parkinson's disease, cognition defects, Downs Syndrome, cerebral hemorrhage with amyloidosis, dementia and head trauma.

40 (original): The method according to claim 36, wherein:

R₁ is a member selected from the group consisting of substituted alkylaryl, substituted aryl, substituted alkyl and substituted heterocyclic groups.

41 (original): The method according to claim 40, wherein:

R₁ is a member selected from the group consisting of:

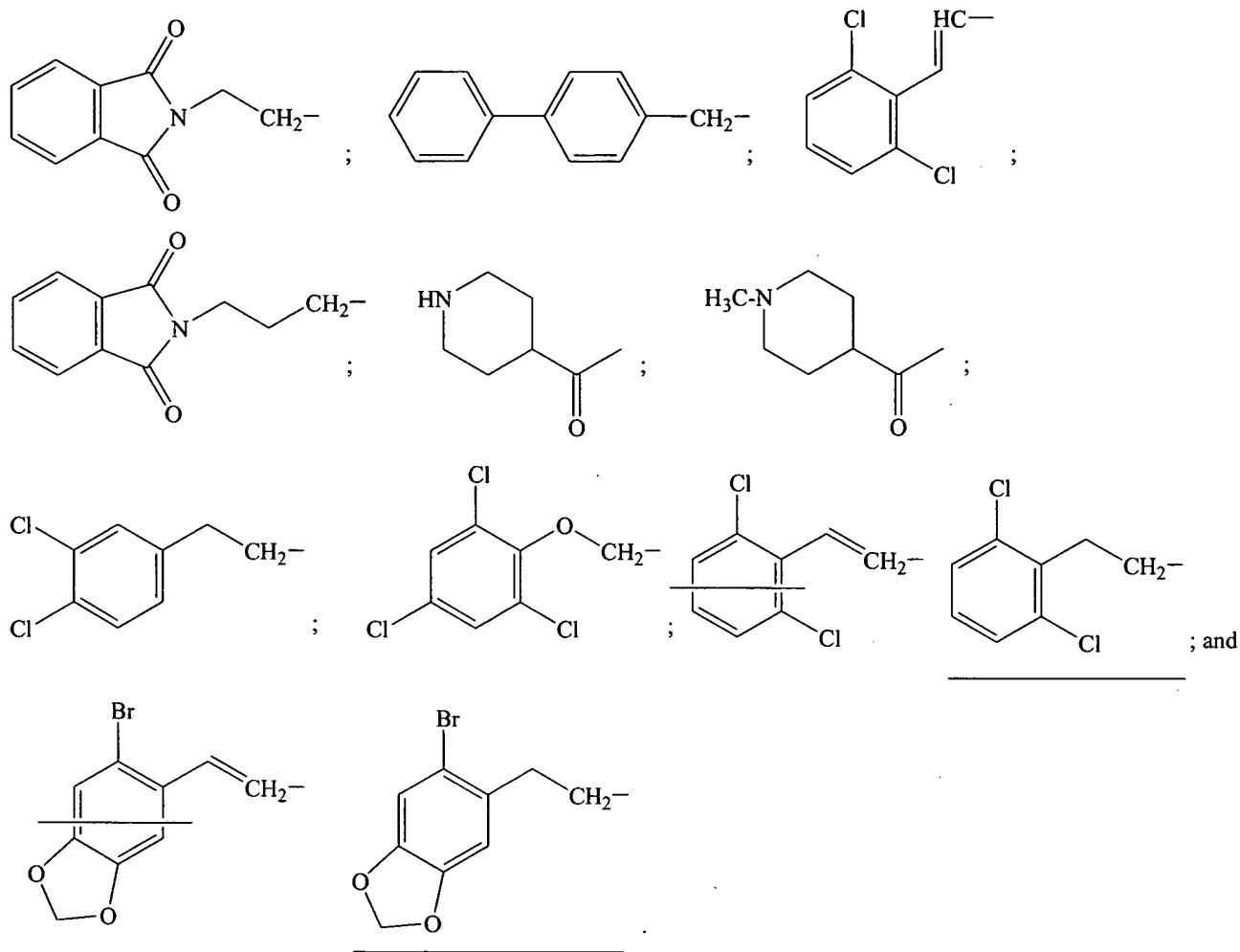


42 (original): The method according to claim 36, wherein:

R₂ is a member selected from the group consisting of substituted alkyl, heterocyclic and substituted heterocyclic groups.

43 (currently amended): The method according to claim 42, wherein R₂ is a

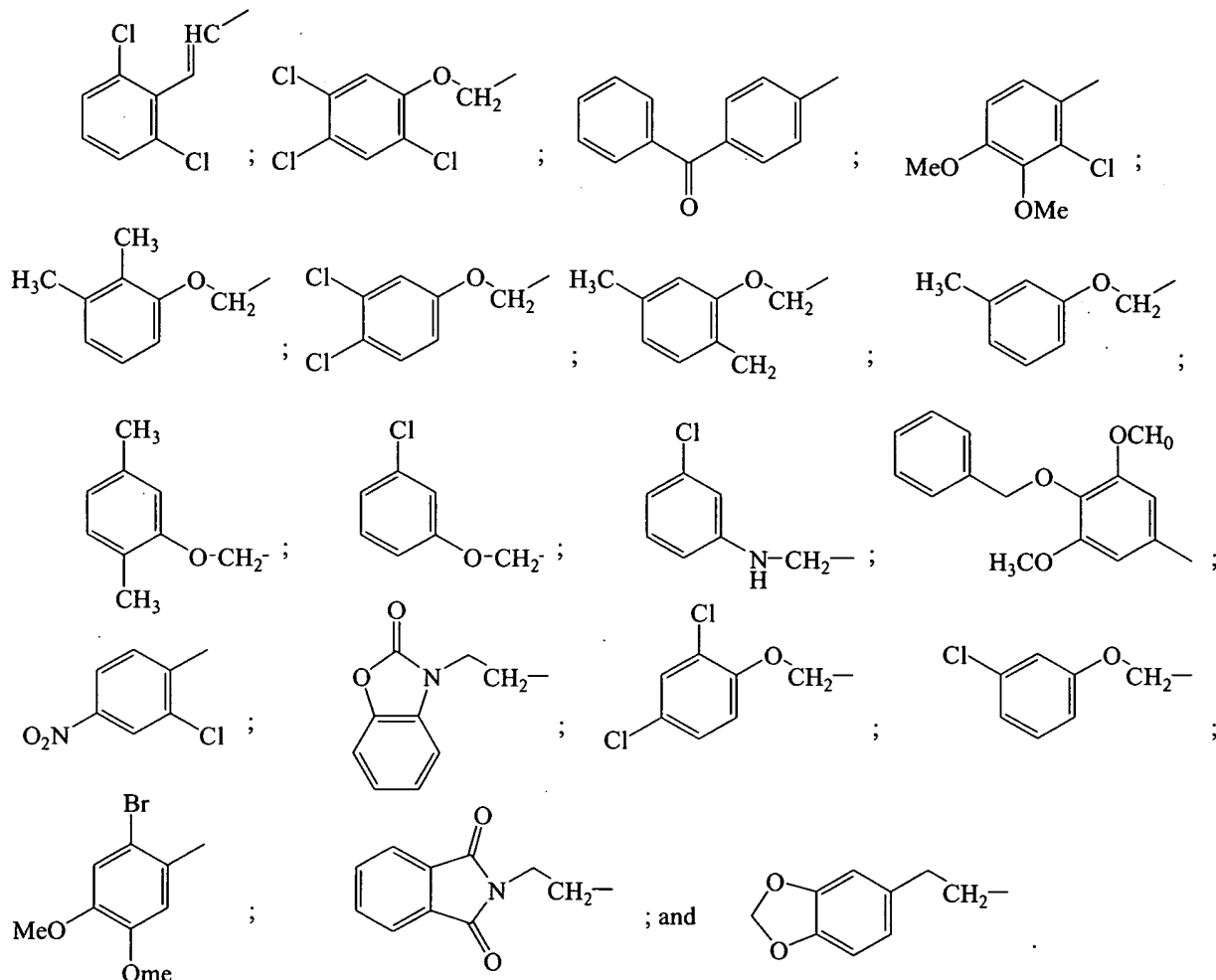
member selected from the group consisting of:



3
4

1 44 (original): The method according to claim 36, wherein:
2 R₃ is a member selected from the group consisting of substituted alkyl and
3 substituted aryl groups.

1 45 (original): The method according to claim 44, wherein R₃ is a member
2 selected from the group consisting of:

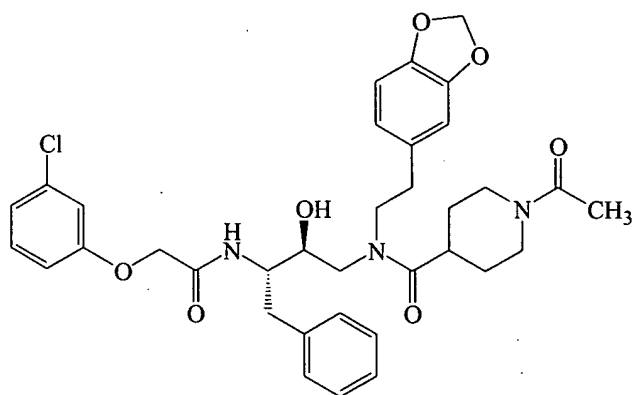


46 (original): The method according to claim 36, wherein R₅ and R₆ and the carbons to which they are bound form an optionally substituted naphthalene ring.

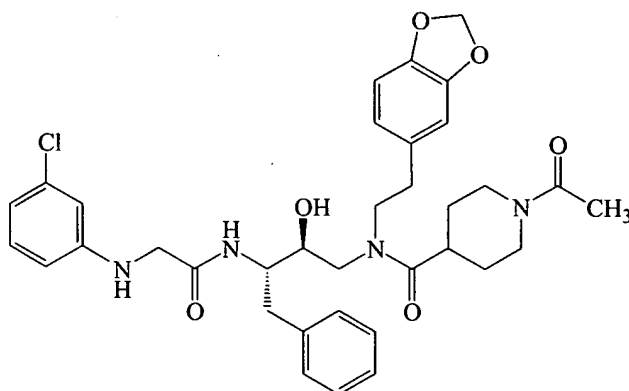
47 (original): The method according to claim 36, wherein R₅ and R₆ are both hydrogen.

48 (original): The method in accordance with claim 36, wherein R₅ is hydrogen and R₆ is meta or para to R₅ and is a member selected from the group consisting of halogen, alkyl, substituted alkyl, aryl, substituted aryl, arylalkyl, substituted arylalkyl, aryloxyalkyl and substituted aryloxyalkyl.

- 1 49 (original): The method in accordance with claim 36, wherein said aspartyl
2 protease inhibitor is a member selected from the group consisting of:

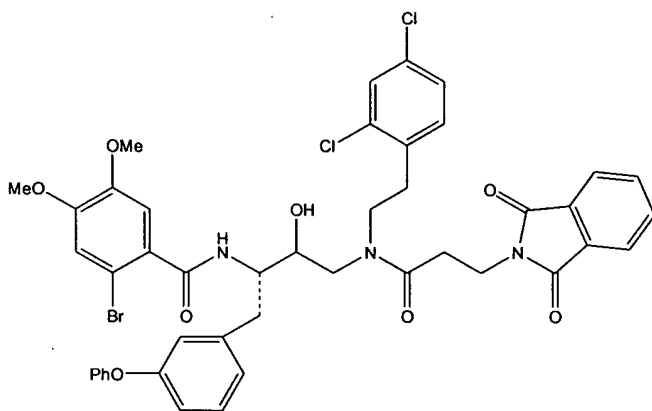


and

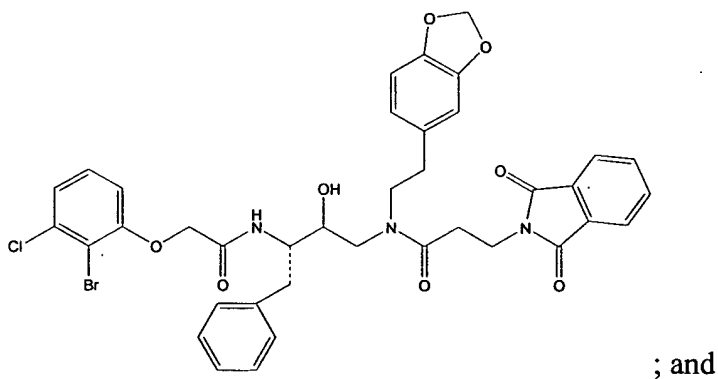


50 (currently amended): The method in accordance with claim 36, wherein said aspartyl protease inhibitor is a member selected from the group consisting of ~~CEL5-A, CEL5-G~~ and ~~EA-1~~, which are illustrated in FIG. 12

CEL5-A having the following structure:



CEL5G having the following structure:



EA 1 having the following structure:

Appl. No. 10/774,262
Amdt. dated June 2, 2005
Reply to Office Action of December 2, 2004

PATENT

